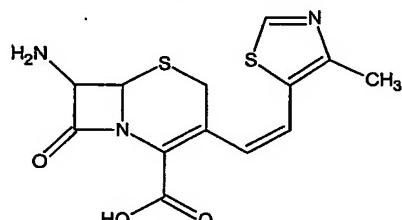
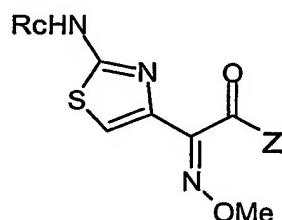


## We Claim:

- 1    1. A process for preparation of cefditoren or a pharmaceutically acceptable salt or  
 2       ester thereof, the process comprising:  
 3           a) reacting a compound of Formula IX with a compound of Formula X  
 4         wherein Z is selected from Formulae Xa, Xb, Xc and Xd and R<sub>c</sub> is selected  
 5         from trityl (triphenylmethyl), acetyl, benzhydryl or acetamidophenyl, R is  
 6         C<sub>1</sub> to C<sub>7</sub> straight or branched chain alkyl, alkenyl, alkynyl or C<sub>6</sub> to C<sub>10</sub> aryl  
 7         or aralkyl, R<sub>1</sub> is C<sub>1-6</sub> straight or branched chain alkyl, cycloalkyl, aryl,  
 8         aralkyl or a heterocycle residue,  
 9           b) isolating cefditoren or pharmaceutically acceptable salt thereof from  
 10      reaction mass, and  
 11           c) optionally converting cefditoren or pharmaceutically acceptable salt thereof  
 12      to a pharmaceutically acceptable ester of cefditoren.



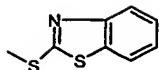
FORMULA IX



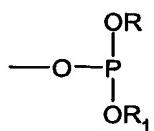
Formula X

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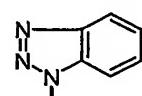
wherein Z is Compound of Formula Xa or Xb or Xc or Xd



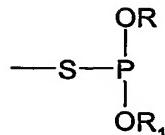
Formula Xa



Formula Xb



Formula Xc



Formula Xd

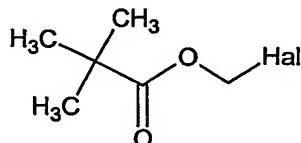
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- 1    2. The process according to claim 1, wherein the compound of Formula IX comprises  
 2       less than 2% of E-isomer.

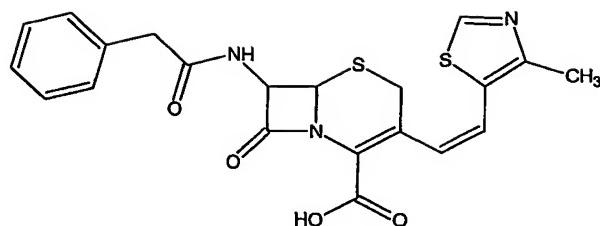
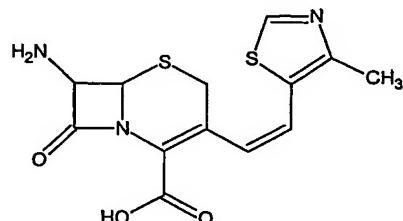
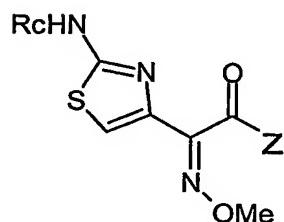
- 1    3.    The process according to claim 1, wherein the compound of Formula X has Z =  
2                    Xa.
- 1    4.    The process according to claim 3, wherein Formula X is *S*-(1,3-benzothiazol-2-yl)-(2-amino-1,3-thiazol-4-yl)(methoxyimino)ethanethioate.
- 1    5.    The process according to claim 1, wherein step a) is carried out in presence of an  
2                    organic solvent.
- 1    6.    The process according to claim 5, wherein the organic solvent is selected from the  
2                    group consisting of chlorinated hydrocarbon such as methylene chloride,  
3                    chloroform, ethylene chloride or ethylene bromide; ethers such as tetrahydrofuran  
4                    and diethyl ether; ketones such as acetone, methyl isobutyl ketone and methyl ethyl  
5                    ketone; alcohols such as methanol, ethanol, propanol, isopropanol and butanol or  
6                    mixtures thereof optionally containing water.
- 1    7.    The process according to claim 1, wherein a base is used in step a).
- 1    8.    The process according to claim 7, wherein the base is an inorganic base or an  
2                    organic base.
- 1    9.    The process according to claim 8, wherein the inorganic base is selected from the  
2                    group consisting of sodium hydroxide, potassium hydroxide, calcium hydroxide,  
3                    magnesium hydroxide, aluminium hydroxide, sodium hydride, potassium hydride,  
4                    sodium carbonate, potassium carbonate, sodium bicarbonate or potassium  
5                    bicarbonate.
- 1    10.   The process according to claim 8, wherein the organic base is selected from the  
2                    group consisting of an organic salt or an organic ammonium compound.
- 1    11.   The process according to claim 10, wherein an organic salt is selected from sodium  
2                    methoxide, potassium t-butoxide or sodium ethoxide.
- 1    12.   The process according to claim 10, wherein an organic ammonium compound is  
2                    selected from triethylamine, dicyclohexylamine or diphenylamine.
- 1    13.   The process according to claim 1, wherein in step b) a salt of cefditoren is isolated.
- 1    14.   The process according to claim 13, wherein a sodium or potassium salt of  
2                    cefditoren is isolated.

- 1    15.    The process according to claim 1, wherein salt of cefditoren is reacted with  
 2           compound of Formula XI, to get cefditoren pivoxil.



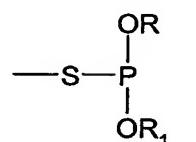
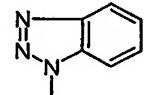
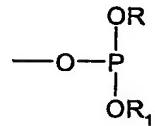
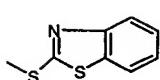
**FORMULA XI**

- 5    16.    A crystalline hydrate of cefditoren sodium.  
 1    17.    A crystalline dihydrate of cefditoren sodium.  
 1    18.    A crystalline cefditoren sodium having about 5.5 to about 7.5% of water by  
 2           weight.  
 1    19.    A crystalline hydrate of cefditoren potassium.  
 1    20.    A crystalline dihydrate of cefditoren potassium.  
 1    21.    A crystalline cefditoren potassium having about 5.5 to 7.5% of water.  
 1    22.    A process for preparation of cefditoren or a pharmaceutically acceptable salt or  
 2           ester thereof comprising:  
 3       a) enzymatically deacylating a compound of Formula VIII to get a compound  
 4           of Formula IX,  
 5       b) reacting the compound of Formula IX with a compound of Formula X  
 6           wherein Z is selected from Formulae Xa, Xb, Xc and Xd, and R<sub>c</sub> is selected  
 7           from trityl (triphenylmethyl), acetyl, benzhydryl or acetamidophenyl, R is  
 8           C<sub>1</sub> to C<sub>7</sub> straight or branched chain alkyl, alkenyl, alkynyl or C<sub>6</sub> to C<sub>10</sub> aryl  
 9           or aralkyl, R<sub>1</sub> is C<sub>1-6</sub> straight or branched chain alkyl, cycloalkyl, aryl,  
 10          aralkyl or a heterocycle residue,  
 11          c) isolating cefditoren or a pharmaceutically acceptable salt thereof from  
 12          reaction mass,  
 13          d) optionally converting cefditoren or the pharmaceutically acceptable salt  
 14          thereof to a pharmaceutically acceptable ester of cefditoren.
- 15

**FORMULA VIII****FORMULA IX****Formula X**

20

wherein Z is Compound of Formula Xa or Xb or Xc or Xd



21

- 1 23. The process according to claim 22, wherein step a) is carried out in water,  
2 optionally containing an organic solvent.
- 1 24. The process according to claim 23, wherein the organic solvent can be water  
2 miscible or water immiscible.

3

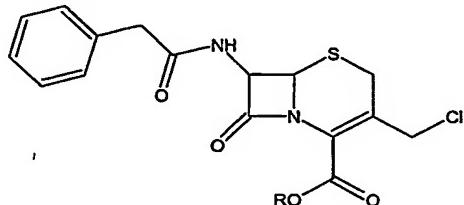
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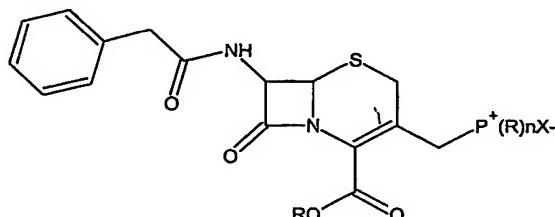
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- 1    25.    The process according to claim 24, wherein the organic solvent is selected from the  
2    group consisting of methanol, ethanol, n-propanol, n-butanol, isopropanol, t-  
3    butanol, methyl formate, ethyl formate, ethyl acetate, n-butyl acetate, isopropyl  
4    acetate, tetrahydrofuran, 1,4-dioxane, diethyl ether, chloroform, methylene  
5    chloride, ethylene chloride, carbon tetrachloride, acetone, methyl isobutyl ketone,  
6    diisobutyl ketone, ethyl methyl ketone, methyl t-butyl ketone.
- 1    26.    The process according to claim 22, wherein pH is maintained between about 5 to  
2    about 8 during step a).
- 1    27.    The process according to claim 26, wherein the pH is maintained by using a base.
- 1    28.    The process according to claim 27, wherein the base is selected from the group  
2    consisting of sodium carbonate, sodium bicarbonate, sodium hydroxide, potassium  
3    hydroxide, potassium bicarbonate, potassium carbonate or water soluble  
4    ammonium compounds such as ammonium hydroxide or triethylamine.
- 1    29.    The process according to claim 22, wherein step a) is carried out using an enzyme  
2    belonging to the class of penicillin acylases or penicillin amidases.
- 1    30.    The process according to claim 29, wherein the enzyme is penicillin G amidase.
- 1    31.    The process according to claim 30, wherein the enzyme is used in immobilized  
2    form.
- 1    32.    A process for the preparation of a compound of Formula IX, comprising:
  - 2       a)    treating a compound of Formula II with an alkali or alkaline earth metal  
3       halide and a phosphorous-containing compound P(YR)<sub>n</sub>, wherein Y is  
4       absent or oxygen or sulphur, n is an integer 2, 3 or 4 and R is selected from  
5       C<sub>1</sub> to C<sub>7</sub> straight or branched chain alkyl, alkenyl, alkynyl or C<sub>6</sub> to C<sub>10</sub> aryl  
6       or aralkyl, in organic solvent, optionally containing water, at a temperature  
7       of about -10 to about 50°C to produce a compound of Formula IV,
  - 8       b)    converting the compound of Formula IV to an ylide of Formula V by  
9       reacting with a base,
  - 10      c)    reacting the ylide of Formula V with 4-methylthiazole-5-carboxaldehyde of  
11      Formula VI in a mixture of organic solvent at a temperature of about -50 to  
12      about 10°C to produce a compound of Formula VII,

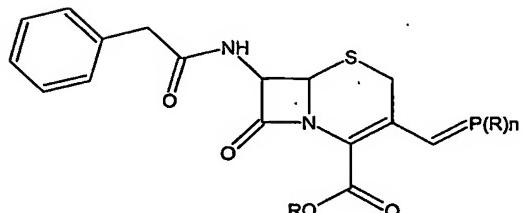
- 13           d) deprotecting the carboxyl functionality of the compound of Formula VII  
14           using phenol or its ether to produce a compound of Formula VIII, and  
15           e) enzymatically deacylating the compound of Formula VIII to produce a  
16           compound of Formula IX.



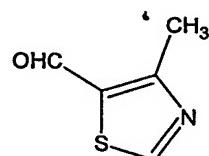
## **FORMULA II**



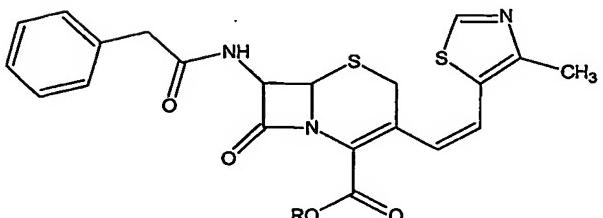
#### **FORMULA IV**



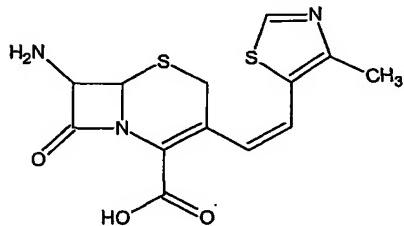
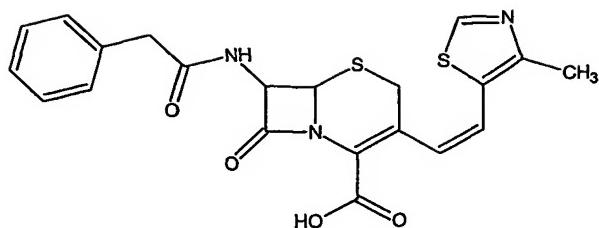
### FORMULA V



## FORMULA VI



### FORMULA VIII



- 1 33. The process according to claim 32, wherein the process is carried out without  
2 isolating any intermediate.
- 1 34. A process for preparation of cefditoren or pharmaceutically acceptable salt or ester  
2 thereof comprising:
- 3 converting a compound of Formula II to a compound of Formula IX,  
4 through intermediates IV, V, VII and VIII with a proviso that the reaction  
5 sequence is carried out without isolating any intermediate,
  - 6 reacting the compound of Formula IX with a compound of Formula X  
7 wherein Z is selected from Xa, Xb, Xc and Xd, and R<sub>c</sub> is selected from  
8 Formulae Xa, Xb, Xc and Xd and R<sub>c</sub> is selected from trityl  
9 (triphenylmethyl), acetyl, benzhydryl or acetamidophenyl, R is C<sub>1</sub> to C<sub>7</sub>  
10 straight or branched chain alkyl, alkenyl, alkynyl or C<sub>6</sub> to C<sub>10</sub> aryl or  
11 aralkyl, R<sub>1</sub> is C<sub>1-6</sub> straight or branched chain alkyl, cycloalkyl, aryl, aralkyl  
12 or a heterocycle residue,
  - 13 c) isolating cefditoren or a pharmaceutically acceptable salt thereof from  
14 reaction mass, and
  - 15 d) optionally converting cefditoren or a pharmaceutically acceptable salt  
16 thereof to a pharmaceutically acceptable ester of cefditoren.
- 1 35. Z-isomer of cefditoren pivoxil having less than 2% of corresponding E-isomer.
- 2

- 1    36.    Z-isomer of cefditoren pivoxil having less than 2% of corresponding E-isomer,  
2                wherein the Z-isomer is isolated from reaction mass without any purification.
- 1    37.    Z-isomer of 7-ATCA having less than 1% of corresponding E-isomer, wherein the  
2                Z-isomer is isolated from reaction mass without any purification.
- 1    38.    Use of the Z-isomer of 7-ATCA according to claim 37 in preparation of cefditoren  
2                or pharmaceutically acceptable salt or ester thereof.